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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,286	08/30/2001	Kiyotada Nunomura	GP104-03.CN1	8507

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EXAMINER
STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/943,286	Applicant(s) NUNOMURA, KIYOTADA
	Examiner Teresa E Strzelecka	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *105,106,108-110 and 116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *105,106,108-110 and 116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicants' response to the Restriction requirement was received on January 21, 2003. Restriction was required for claims 1-55, which were no longer pending in the case, being cancelled by a preliminary amendment, which was not entered into the case prior to mailing of the restriction requirement.

2. Applicants cancelled the pending claims 56-104, 107 and 111-115, amended claim 105 and added a new claim 116. Therefore claims 105, 106, 108-110 and 116 are pending and will be examined.

Information Disclosure Statement

3. The information disclosure statement filed on January 8, 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the reference of Wong-Staal et al. does not have a proper place and date of publication, since it was printed from an Internet site, and these sites change with time. It has been placed in the application file and the remaining references were considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Before proceeding with the rejection, Applicants' definition of a "pseudo target" is provided (page 8, lines 8-14):

"A "pseudo target" is a polynucleotide that can be co-amplified with the analyte polynucleotide in a single amplification reaction. The pseudo target and the analyte polynucleotide may be amplified using the same set of oligonucleotide primers. However, it is also possible for the pseudo target and the analyte polynucleotide to co-amplify using independent primer sets. The pseudo target and the analyte polynucleotide will be nonidentical molecules so that the analyte polynucleotide and the pseudo target can be distinguished from each other."

Therefore, a pseudo target according to this definition can be any polynucleotide which is co-amplified with the target polynucleotide.

6. Claims 105, 106 and 116 are rejected under 35 U.S.C. 102(e) as being anticipated by Aoyagi et al. (U. S. Patent No. 5,952,202).

Regarding claims 105 and 106, Aoyagi et al. real-time detection of nucleic acids by co-amplification of the target polynucleotide with an internal control polynucleotide (ICP). The target and internal control polynucleotides are amplified with their respective primers. The amplification products are detected with probes specific for the target and internal control, respectively (col. 7, lines 16-35). The probes are self-quenching fluorescence probes, which have a reporter dye and quencher dye attached to the opposite ends of the probes. During the polymerization reaction the polymerase digests the probes to separate the reporter dye from the quencher dye, and the increased

fluorescence indicates the presence of amplified products (col. 8, lines 10-41; Fig. 1; col. 14, lines 45-63).

The signal may detected as a Ct value, which indicates the presence of a fluorescence signal distinguishable from the background, indicating presence of a target polynucleotide in the sample (col. 18, lines 45-61). Aoyagi et al. teach detection of *Mycoplasma* DNA by a process comprising co-amplification of *Mycoplasma* cDNA and an internal control polynucleotide using *Mycoplasma*-specific probe labeled with FAM (target) and JOE (control). The pre-determined threshold Ct value of 40 indicates that there is no detectable DNA in the sample, whereas Ct values below 40 indicate presence of the target and control polynucleoties (col. 21, lines 25-36; col. 36, lines 1-26; Fig. 9).

Regarding claim 116, Aoyagi et al. teach detection of the signal using a fluorescence detection system comprising a lens, a fiber optic and a CCD camera (col. 17, lines 63-67; col. 18, lines 1-42).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 109 and 110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aoyagi et al. as applied to claim 105 above, and further in view of Jurriaans et al. (Immunol. Letters, vol. 51, pp. 15-22, 1996).

A) Claim 109 is drawn to analyte polynucleotide being a viral polynucleotide, and claim 110 is drawn to the viral polynucleotide being an HIV-1, HIV-2, HBV or HCV polynucleotide.

B) Teachings of Aoyagi et al. are described above. Regarding claims 109 and 110 Aoyagi et al. teaches application of the methods to target-specific assays for pathogen detection, which can be performed in a multiplex format (col. 11, lines 30-47). Aoyagi et al. do not explicitly teach detection of HIV-1, HIV-2, HBV or HCV.

C) Jurriaans et al. teach determination of the amounts of HIV-1 RNA and DNA in clinical samples by amplification methods including NASBA and PCR. It was found that the levels of viral RNA and DNA measured over a period of time can serve as indicators of whether and how fast the disease will develop (Fig. 2, 3; pages 18-21). In particular, the levels of single-LTR DNA may be valuable in detecting early signals of the spread of the infection (page 20, the last paragraph, continued on page 21). In addition, monitoring of single-LTR DNA enables accurate monitoring of e response to antiviral therapy (page 21, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the method of Aoyagi et al. for the detection of HIV-1 DNA of Jurriaans et al. The motivation to do so, provided by Aoyagi et al., would have been that using real-time amplification with internal controls provide a rapid and accurate nucleic acid amplification assay (Abstract).

9. Claims 105, 106, 108-110 and 116 are rejected under 35 U.S.C. 103(a) as being unpatentable over van Gemen et al. (J. Virol. Methods, vol. 49, pp. 157-168, 1994; cited in the IDS of the parent application, 09/620,958).

Before proceeding with the rejection, a bases for the rejection is presented:

MPEP 2144.04 [R-1] Legal Precedent as Source of Supporting Rationale

III. AUTOMATING A MANUAL ACTIVITY

In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the known pressure valve system to release the inner core after a predetermined time has elapsed." The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.).

Regarding claims 105, 106, 109 and 110, van Gemen et al. teach co-amplification of HIV-1 target RNA (WT) with three internal standards, Q_A, Q_B and Q_C, which also contained HIV-1 sequences. The internal standards were added to the amplification sample in different amounts, covering a certain concentration range, for example, from 10^2 to 10^4 molecules. Amplification was performed with two primers, and the amplification products were detected with probes specific for either the target HIV or standard amplicons. The amount of target RNA can be calculated from the ratio of WT and Q_A, Q_B and Q_C signals (page 158, 159; page 160, the last paragraph, continued on page 161). The threshold of detection is 10^3 molecules per 0.1 mL plasma. Quantitation of HIV-1 RNA was performed for three HIV-1 infected patients using that threshold, and it was determined that patient 2 was positive, and patient 3 had RNA amount below the quantitation limit (page 163; Table 2).

Regarding claims 108 and 116, van Gemen et al. teach detection of the amount of probe hybridized to the WT or internal standard DNA by quantifying the amount of luminescence of an ECL-labeled (electrochemiluminescent) probe in a luminometer (page 158, paragraphs 3 and 4; page 160, fifth paragraph). Van Gemen et al. teach automated detection of the ECL labels (page 166, the last paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to automate the detection of a pre-determined amount of HIV-1 RNA based on the semi-automated detection method of van Gemen et al. The motivation to do so, provided by van Gemen et al., would have been that one-tube reaction could be performed in large numbers, facilitating large studies of HIV-1 viral load (page 166, the last sentence).

10. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

May 5, 2003

Teresa Strzelecka, Ph. D.

Patent Examiner

Teresa Strzelecka
05/05/03